mixing the analyte, a specific binding partner for the analyte and the labeled immunoreactant to form a mixture;

irradiating the mixture with a single photon of light having a wavelength ranging from 400 nm to 1000 nm;

measuring the emitted luminence from the mixture; and

detecting an analyte using said luminence measurement.

REMARKS

This amendment is responsive to the final rejection dated August 14, 2001 in the above-identified application.

Claim 1, 4, 6, and 9-10 have been amended. Claims 1-14 are currently pending in the present application.

Claims 1-4, 6 and 8-14 have been rejected under 35 U.S.C. §112, second paragraph as being indefinite. The specific detailed rejections are addressed below.

In claim 1, line 11, the applicant has adopted the Examiner's suggestion to change "luminance" to "luminence" in order to overcome this rejection.

Claims 1 and 10 have been rejected as incomplete for omitting a detection step. Claims 1 and 10 have been amended in order to further require the step of: "detecting an analyte using said luminence measurement." It is considered that this amendment overcomes the rejection of claims 1 and 10.

Claim 4 was rejected as indefinite for reciting "complexing ability" in line 4 of the claim. Claim 4 has been amended to require that the various moieties can complex with the various ions

recited in the claim. It is considered that this amendment renders claim 4 definite since a skilled person can run a simple test to determine whether a particular moiety can complex with a particular ion and therefore can routinely determine the scope of the present claim 4, as amended. Accordingly, favorable consideration and withdrawal of the rejection of claim 4 in view of the amendment is requested.

Claims 6 and 9 have been rejected on the basis that they require that the detector be capable of detecting luminescence in a particular wavelength range. Claims 6 and 9 have been amended to require a detector which can detect luminescence in a particular wavelength range. It is considered that this amendment overcomes the rejection. More specifically, a skilled person can, using a routine test, determine whether a particular detector can detect luminescence in a particular wavelength range. Thus, as a routine matter for a skilled person to determine whether a particular detector meets this limitation of the claim. For this reason the claims 6 and 9 are definite. Favorable consideration and withdrawal of the rejection is requested.

Claim 10 has been rejected on the basis that luminence is misspelled in line 11. The spelling error has been corrected as suggested by the Examiner. In addition, claim 10 has been rejected as vague and indefinite in reciting "in contact" because it is unclear and fails to specifically define what is encompassed by the term "contact." This rejection is respectfully traversed and reconsideration is requested. More specifically, this limitation is explained on page 4, lines 5-12 of the specification. It is a routine matter for a skilled person to determine if a sensitizer is in contact with a ligand. Moreover, the specification explains one example of being "in contact", namely, where the sensitizer includes a site which can act as the complexing moiety. Accordingly, since it is a routine matter to determine the metes and bounds of claim 10,

claim 10 is considered to be sufficiently definite to meet the requirements of 35 U.S.C. §112. Favorable consideration and withdrawal of the rejection is requested.

Claim 12 was rejected for the same reason as claim 10, namely that it employed the terminnology "in contact". The same argument applies to claim 12. Favorable consideration and withdrawal of the rejection is requested.

Claims 13-14 have been rejected as vague and indefinite in reciting the term "attached." This rejection is respectfully traversed and reconsideration is requested for the reasons which follow.

More specifically, it is submitted that the term "attached" is sufficiently definite for a person of ordinary skill in the art to be able to routinely determine whether a particular specific binding partner or immunoreactant are attached to a carrier by applying a simple test. The term "attached" should be given its common meaning to a person of ordinary skill in the art. For example, such a test is clearly disclosed in the specification on page 10, lines 8-14. The specification also gives further details regarding examples of attachments in this paragraph. Accordingly, in view of these facts, it is submitted that "attached" is sufficiently definite such that a skilled person can determine the scope of claims 13-14. For these reasons, withdrawal of the rejection of the claims 13-14 is requested.

Finally, claims 13-14 have been rejected on the basis that it is unclear whether the "the specific binding partner" and the "immunoreactant" are each attached to the same carrier or each attached to a separate carrier. Claims 13-14 only require that the specific binding partner and immunoreactant be attached to a carrier. The way the claims read now it can encompass either the situation where both the specific binding partner and the immunoreactant are attached to the same carrier or the situation where the specific binding partner and the immunoreactant are

attached to two different carriers. This does not render the scope of claims 13-14 indefinite since a person with skill in the art can determine using a routine test whether the specific binding partner or the immunoreactant are attached to a carrier and therefore can determine the meets and bounds of claims 13-14. Accordingly, favorable consideration and withdrawal of the rejection of claims 13-14 is requested for these reasons.

Claims 1-14 have been rejected under 35 U.S.C. §102(e) as being anticipated by U.S. Patent No. 6,159,686 (Kardos et al.). This rejection, at least insofar as it applies to claims 1-14, as amended, is respectfully traversed and reconsideration is requested for the reasons which follow.

Claims 1-14, as amended, relate to the methods and apparatus for detection of an analyte in a test sample. In the method, a lanthanide ion-ligand complex is prepared by contacting a lanthanide ion and a ligand comprising, or in contact with, a sensitizing moiety which absorbs light in the 400-1000 nanometer region. An immunoreactant is labeled with the lanthanide ion-ligand complex by contacting the immunoreactant with the lanthanide ion-ligand complex to form a labeled immunoreactant. An analyte, a specific binding partner for the analyte and a labeled immunoreactant are mixed to form a mixture and the mixture is irradiated with light having a wavelength ranging from 400 nanometers to 1000 nanometers using a single photon. Finally, the emitted luminence of the mixture is measured and an analyte is detected using the luminence measurement.

The present invention comprises a specific binding partner for the analyte, an immunoreactant and a label which is a lanthanide ion-ligand complex, wherein the ligand comprises, or is in contact with, a sensitizing moiety which absorbs light in the 400-1000 nanometer range. The present invention also includes an apparatus for detection of an analyte

comprising the kit as claimed, a light source for omitting a single photon in the 400-1000 nanometer range and a detector which can detect luminescence in the 800-1600 nanometer range.

Kardos, et al., discloses a two-photon process, which is unmistakably indicated in lines 32-34 of column 30 of Kardos, et al. The Examiner took the position on page 8 of the final rejection that Kardos, et al. discloses using only one light source for irradiation at 1000 nanometers at column 28, lines 45-52. From this, the Examiner concludes that Kardos, et al. discloses a single photon process. This is incorrect as can be clearly seen from the disclosure of Kardos, et al. at column 30, lines 29-34 where it is clearly disclosed that using a single light source, namely, a pump laser, the goal is to excite the second excited single state in a dye with a pulse from a tunable dye laser using two photons. Thus, the fact that Kardos, et al., discloses using a single light source does not mean that Kardos, et al. uses a single photon. Contrary to this conclusion, Kardos, et al., et al. clearly teaches that at least a two photon process is employed.

In addition, to support Applicants' position, Applicant encloses herewith a declaration of Dr. Clemens Brunner, an expert in the area of photoluminescence. Mr. Brunner points out clearly at page 2 of his declaration that Kardos, et al. teaches a two-photon process whereas the present invention relates to a single photon process. Accordingly, it is considered that the present invention is clearly novel over Kardos, et al. because it employs a single photon process and because Kardos, et al. does not disclose or suggest a one photon process using light with a wave length in the range of 400-1000 nanometers. Favorable consideration and withdrawal of the rejection under 35 U.S.C. §102(e) is requested.

Claims 1-14 have been rejected under 35 U.S.C. §103(a) as being unpatentable over U.S. Patent No. 5,830,769 (Weider, et al.) in view of Kardos, et al. This rejection, at least insofar as it

applies to claims 1-14, as amended, is respectfully traversed and reconsideration is requested for the reasons which follow.

The Examiner takes the position that Weider, et al. discloses all of the limitations of claim 1 except for the specific ranges of light wavelengths of excitation. The Examiner then relies on Kardos, et al. for disclosing the specific ranges of light wavelengths of excitation claimed in claim 1 of the present application. More specifically, the Examiner relies on the disclosure in Weider, et al. of sensitizing moieties which are similar to those disclosed in the present application as the basis of concluding that Weider, et al. discloses all of the elements of claim 1 except the specific ranges of light wavelengths. Dr. Brunner, in the enclosed declaration, addresses this point by pointing out that the long wavelength organic molecules disclosed in Weider, et al. such as fluorescein, rhodamine and phycobiliproteins are used to sensitize the luminescence of the lanthanide. This is a totally different use than in the present invention and therefore does not indicate that Weider, et al. employs light of the wavelength range which is claimed by claim 1.

Rather, as Dr. Brunner points out, it is necessary to use wavelengths in the ultraviolet region, i.e. below 400 nanometers wave length, to excite the therbium and europium lanthanide ions of Weider, et al. In fact, Dr. Brunner points out that Weider, et al. suffers from the limitation that the second fluorophore emits in the visible part of the spectrum and it is this limitation of europium and therbium emitters that is solved by the present invention.

not recited in claim 1 *

A second difference of the approach of the present invention is that the sensitizing moiety which absorbs in the range of 400-1000 nanometers is directly connected or in contact with the lanthanide ion. This is important since the energy transfer between the sensitizing moiety and the lanthanide ion is distance dependent. Thus, the present invention is optimized for energy transfer

whereas in Weider, et al. the sensitizers relied upon by the Examiner are added to the solution as a separate component and are not connected to or in contact with the lanthanide complex.

For these reasons it is considered that there are clear differences between the present invention and Weider, et al. and that the teachings of Weider, et al. would lead a person of skill in the art to employ wavelengths of excitation below 400 nanometers even if the teachings of Kardos, et al. were considered since the lanthanides europium and therbium suggested by Weider, et al. cannot be excited at wavelengths above 400 nanometers. See affidavit of Dr. Brunner.

Finally, as mentioned above, the Kardos, et al. reference does not disclose a single photon excitation process. Therefore, it is inappropriate to combine Kardos, et al. and Weider, et al. since none of the materials in Weider, et al. can be excited above 400 nanometers wherein all of the materials of Kardos, et al. require wave lengths in excess of 400 nanometers for excitation. Weider, et al. and Kardos, et al. relate to two totally different systems which cannot be readily combined with one another in the manner that the Examiner suggests.

For the foregoing reasons, favorable consideration and withdrawal of the rejection under 35 U.S.C. §103(a) of claims 1-14 as unpatentable over Weider, et al. in view of Kardos, et al. is respectfully requested.

Respectfully submitted,

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1. (Three Times Amended) A method for detection of an analyte in a test sample comprising the steps of:

preparing a lanthanide ion-ligand complex by mixing a lanthanide ion and a ligand, wherein the lanthanide ion is selected from the group consisting of neodymium (III) ion, ytterbium (III) ion (Yb3+) and erbium (III) ion (Er^{3+}), and wherein said ligand comprises a sensitizing moiety, which absorbs light in the 400 –1000 nm region; not in contact?

labeling an immunoreactant with the lanthanide ion-ligand complex by contacting the immunoreactant with the lanthanide ion-ligand complex to form a labeled immunoreactant;

? mixing an analyte, a specific binding partner for the analyte, and the labeled immunoreactant to form a mixture; → interaction between 3 components? i.e. binding vs unbinding

irradiating the mixture with a single photon of light having a wavelength ranging from 400 nm to 1000 nm; [and]

measuring an emitted [luminance] luminence from said mixture; and detecting an analyte using said luminence measurement. wherein luminescence from said mixture is indicative of the presence of analyte.

4. (Three Times Amended) The method as claimed in any one of claims 1 and 10, wherein the ligand is a composition which comprises, as one of its constituents, a compound which comprises an element selected from the group consisting of oxygen, nitrogen, phosphorous, and sulfur moieties which [have complexing ability towards] can complex with Nd (III), Yb (III), or Er (III) ions, and the sensitizing moiety is selected from [selected from] the group consisting of fluoresce in derivatives; triphenylmethane derivatives; porphyrin derivatives; rhodamine derivatives; phenothiazine derivatives; phenoxazine derivatives; coumarin

derivatives; acridin derivatives; thio-indigo derivatives; indigo derivatives; carbocyanine derivatives; squaraine derivatives; [and] naphthalocyanine derivatives; <u>and</u> phthalocyanine derivatives.

6. (Three Times Amended) An apparatus for detection of an analyte in a test sample comprising:

the kit of claims 5,12, 13 or 14;

a light source <u>for emitting a single photon</u> in the 400-1000 nm <u>wavelength</u> range; and

a detector, which [is capable of detecting] <u>can detect</u> luminescence in the 800-1600 nm <u>range</u>.

9. (Twice Amended) The apparatus as claimed in claim 6, wherein the detector [is capable of detecting] <u>can detect</u> luminescence in the 800-1100 [*nm*] <u>nm</u> range.

10. (Amended) A method for detection of an analyte in a test sample comprising the steps of:

preparing a lanthanide ion-ligand complex by mixing a lanthanide ion and a ligand, wherein the lanthanide ion is selected from the group consisting of neodymium (III) ion, ytterbium (III) ion (Yb^{3+}) and erbium (III) ion (Er^{3+}), wherein the ligand is in contact with a sensitizing moiety, which absorbs lights in the 400 –1000 nm [region] <u>range</u>;

labeling an immunoreactant with said lanthanide ion-ligand complex by

contacting the immunoreactant with the lanthanide ion-ligand complex to form a labeled immunoreactant[.];

mixing the analyte, a specific binding partner for the analyte and the labeled immunoreactant to form a mixture;

irradiating the mixture with a single photon of light having a wavelength ranging from 400 nm to 1000 nm; [and]

measuring the emitted [luminance] luminence from the mixture; and detecting an analyte using said luminence measurement.